REMARKS

I. Support for the Amendments

Claims 1-8, 11, and 17 are presently in the application. Claims 1-6, 8, and 11 have been amended, and new claim 17 has been added. Claims 15 and 16 have been canceled without prejudice to their pursuit in an appropriate continuation or divisional application.

Support for amended claims 1-6, 8 and 11 and for new claim 17 can be found in the original specification and claims.

Additional support for amended claims 1 and 4 can be found, e.g., from page 14, line 19, to page 15, line 2; and in the Examples. Additional support for amended claim 8 can be found, e.g., from page 15, line 20, to page 16, line 3; and in the Examples. The amendments to claims 2, 3, 5, and 6 are largely a matter of form. Additional support for amended claims 1-4 and 11 can be found, e.g., on page 14, lines 5-14; from page 15, line 3, to page 17, line 31; and in the Examples. Additional support for amended claim 8 can be found, e.g., on page 15, lines 20-26; from page 15, line 3, to page 17, line 31; and in the Examples. Additional support for amended claims 7 and 11 and for new claims 17 can be found, e.g., from page 16, line 4, to page 17, line 31; from page 15, line 3, to page 17, line 31; and in the Examples. Additional support for new claim 17 can be found, e.g., on page 5, lines 9-17; from page 9, line 30, to page 10, line 4; from page 15, line 34, to page 16, line 3; on page 16, lines 22-25; in Figs. 7 and 8; and in the Examples.

II. Status of the Claims

Claims 1-14 were originally in the application, with claim 1 being the independent claim. Claims 1-14 were subject to an Election/Restriction Requirement, and claims 1-8 and 11 (Group I) were elected with traverse.

In the Office Action mailed January 13, 2004, the Examiner rejoined claims 9-10, but stated that the restriction requirement remains in force for claims 12-14. The Examiner rejected claims 1-11, which were all the remaining claims. Claims 1-11 were pending in the application, with claim 1 being the independent claim.

Previously, claims 1-8 and 11 were in the application. Claims 1 and 11 were the independent claims. Claims 9-10 and non-elected claims 12-14 were canceled without prejudice to their pursuit in an appropriate continuation or divisional application.

Claims 1-8, 11, and 17 are currently in the application. Claims 1-6, 8, and 11 have been amended and new claim 17 has been added. Claims 2-8 are dependent on claim 1, and claim 17 is dependent on claim 11. Claims 15 and 16 have been canceled without prejudice to their pursuit in an appropriate continuation or divisional application.

III. The Objection to the Specification is Accommodated

The Examiner has objected to the specification under 35 U.S.C. §132, alleging that it introduces new matter into the disclosure. Applicants have amended the specification and respectfully request withdrawal of the objection.

IV. The Rejection of Claims 1-8, 11, and 15-16 under 35 U.S.C. §112, Second Paragraph is Accommodated in Part and Rendered Moot in Part

The Examiner has rejected claims 1-8, 11, and 15-16 under 35 U.S.C. §112, second paragraph (pp. 3-5).

The Patent Office alleges the following new rejections:

> Claims 2-3 are vague and indefinite in that the metes and bounds of the phrase "wherein the regulator sequence is" are unclear. It is unclear whether the term **"is"** is necessarily closed language or not. It would be remedial to amend the claim to include language that is explicitly open (e.g. comprising) or closed (e.g. consisting of) with regard to the presence of additional elements.
>
> Claim 4 is vague and indefinite in that the metes and bounds of the phrase "or a fragment thereof" are unclear. It is unclear if the term refers to the base sequence comprising nucleotides 1-2270 of SEQ ID NO: 1 or solely refers to nucleotides 1-2270 of SEQ ID NO: 1.
>
> Claim 5 recites the limitation of a recombinant vector "containing the DNA described in claim 1". There is no clear and positive prior antecedent basis for the term "the DNA described in claim 1" since there are several different DNAs described in the claim (e.g. the DNA sequences recited in parts (a)-(d)). In addition, the term "containing" is not explicitly defined in the instant specification and it is not clear whether the term is meant to be open (e.g. comprising) or closed language (e.g. consisting of), making the metes and bounds of the DNA claimed unclear. It would be remedial to amend the claim to include language that is explicitly open (e.g. comprising) or closed (e.g. consisting of) with regard to the presence of additional elements.
>
> Claim 8 is vague and indefinite in that the metes and bounds of the phrase "method for screening for a compound....characterized by measuring and comparing" are not clear. It is unclear as the claim is currently written whether one necessarily performs the recited positive action steps or not. It would be remedial to amend the claim language to recite a "method for screening for a compound....comprising measuring and comparing".
>
> There is no clear and positive prior antecedent basis in claim 11 for the term "the UCP-2 promoter sequence". Nor are the metes and bounds of this term clear as no particular sequence is disclosed in the specification as being "the" UCP-2 promoter sequence and there does not appear to be such a canonical sequence disclosed in the art. [Pp. 3-4; emphasis in original.]

The Patent Office has also maintained the following rejection of claim 1:

> Claim 1 recites the limitation of an isolated DNA "containing" a regulator sequence. The term "containing" is not explicitly defined in the instant specification and it is not clear whether the term is meant to be open (e.g. comprising) or closed language (e.g. consisting of), making the metes and bounds of the DNA claimed unclear. It would be remedial to amend the claim to include language that is explicitly open (e.g. comprising) or closed (e.g. consisting of) with regard to the presence of additional elements.
>
> Claim 1 lacks an article (e.g. "a" or "the") prior to the term "uncoupling protein-2 (UCP-2) promoter region" in line 1. The lack of such an article prior to the term makes it unclear as to how many UCP-2 promoter regions are to be present in the claimed nucleic acid.
>
> Claim 1 is vague and indefinite in that the metes and bounds of the phrase "wherein the regulator sequence is a sequence selected from" are unclear. It is unclear whether the term **"is"** is necessarily closed language or not. It would be remedial to amend the claim to include language that is explicitly open (e.g. comprising) or closed (e.g. consisting of) with regard to the presence of additional elements. [Pp. 4-5; emphasis in original.]

Claims 15 and 16 have been canceled without prejudice, and Applicants respectfully submit that the rejection is rendered moot with respect to these claims.

With respect to the above remarks concerning claims 1-8, the language of claim 1 presently reads as follows:

> 1 (currently amended). An isolated DNA comprising an uncoupling protein-2 (UCP-2) promoter region, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of:
>
> a. a peroxisome proliferator response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;
> b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;
> c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030

of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1.

Applicants respectfully submit that the present claim 1 addresses all of the Examiner's remarks. Claims 2-8 are dependent on claim 1, and the amended language of claim 1 also applies to these claims. Applicants have also amended claims 2-5 and 8 to accommodate the Examiner's additional remarks concerning those claims as well.

The language of claim 11 presently reads as follows:

11 (currently amended). A kit for screening for a compound or its salt that promotes or inhibits UCP-2 promoter activity, which comprises:

a. a medium for culturing a host animal cell line;

b. a plasmid for measurement of UCP-2 promoter activity comprising:

i. plasmid DNA carrying a UCP-2 promoter sequence which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, which the part of the base sequence comprises a regulator sequence selected from the group consisting of:

(a) a peroxisome proliferators response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;

(b) a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1

(c) a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nuelcotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

(d) a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1; and

ii. a structural gene inserted downstream of the UCP-2 promoter; and

c. a host animal cell line.

Applicants respectfully submit that the present claim 11 addresses all of the Examiner's remarks and clearly delineate the metes and bounds of claimed invention with respect to the UCP-2 promoter sequence.

Applicants respectfully submit that the present amendments to claims 1-6, 8, and 11 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph, thereby placing these claims in condition for allowance.

V. The Rejection of Claims 1-8, 11 and 15-16 Under 35 U.S.C. §112, First Paragraph, is Traversed, but Accommodated, in Part and Rendered Moot in Part

A. Rejection of Claims 11 and 15-16 Alleging New Matter

The Examiner has rejected claims 11 and 15-16 under 35 U.S.C. §112, first paragraph (pp. 5-7). Applicants respectfully disagree.

The Patent Office alleges:

> Claims 11 & 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by the amendment of the claims in the response filed 12/22/2004. This is a New Matter rejection.**
>
> Claim 11 has been amended to broadly recite new limitations with regard to the constituent parts of a kit including: a cell culture medium, a cell differentiation medium and a plasmid for measurement of UCP-2 promoter activity. Claim 11(a) is broad in that it recites a culture medium comprising DMEM supplemented with *any* concentration of fetal calf serum. Claim 11(b) is broad in that it recites a cell differentiation medium comprising DMEM supplemented with *any* concentration of rabbit serum. Claim 11(c) is broad in

that it recites that the pGL-3-basic plasmid carries "the" UCP-2 promoter sequence. Claim 11(d) recites a host cell line "comprising" an MG-63 cell line.

The portion of the specification pointed to by applicants' response as providing support for the amendments to claim 11 and for new claims 15-16 recites a very specific composition for the claimed kit that is narrower in scope than what is recited in claims 11, 15 & 16 (e.g. see pages 15-17 of the instant specification). For example, the cell culture medium is described as DMEM supplemented with 10% fetal calf serum. The cell differentiation medium is described as DMEM supplemented with 5% rabbit serum. The pGL3-basic plasmid is described as comprising a UCP-2 promoter sequence of the invention operatively linked to a structural gene. The host cell line is described as being MG-63 cells. The specific example pointed to by applicants' response only provides support for the very specific example and does not provide support for claiming the components of the kit more broadly. For example, there is no support for claiming literally any percentage of FCS or rabbit serum in the cell culture or differentiation media. There is no support in the cited section for claiming "the" UCP-2 promoter as no such canonical promoter has been defined in the specification. There is no support in the cited portion of the specification for claiming a cell line "comprising" an MG-63 cell line. Nor can the examiner find implicit or literal support in the remainder of the originally filed specification and claims for the newly added subject matter cited above. Therefore, each of the newly added limitations is impermissible New Matter. [Pp. 5-7; emphasis in original.]

Claims 15 and 16 have been canceled without prejudice, and Applicants respectfully submit that the rejection is rendered moot with respect to these claims.

Applicants respectfully disagree, but have amended claim 11. The language of claim 11 presently reads:

11 (currently amended). A kit for screening for a compound or its salt that promotes or inhibits UCP-2 promoter activity, which comprises:

a. a medium for culturing a host animal cell line;

b. a plasmid for measurement of UCP-2 promoter activity comprising:

i. plasmid DNA carrying a UCP-2 promoter sequence which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, which the part of the base sequence comprises a regulator sequence selected from the group consisting of:

(a) a peroxisome proliferators response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;
(b) a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1
(c) a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nuelcotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and
(d) a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1; and

ii. a structural gene inserted downstream of the UCP-2 promoter; and

c. a host animal cell line.

Applicants respectfully submit that the composition of the kit described in the specification is merely an exemplification of one embodiment of each element described. It is believed that the Examiner is referring, in part, to the following passage:

(2) A kit for screening a compound or its salt that promotes or inhibits UCP-2 promoter activity (e.g. a compound that promotes or inhibits heat production)

A kit for determining a compound or its salt that promotes or inhibits UCP-2 promoter activity (e.g. a compound that promotes or inhibits heat production) is characterized by use of the transformant described above.

Examples of the kit for determining a compound or its salt that promotes or inhibits UCP-2 promoter activity of this invenstion are as follows.

① Screening reagents

1. Cell culture medium

Dulbbecco's modified Eagle's medium (Gibco Co.) supplemented with 10% fetal calf serum (Gibco Co.)

2. Cell differentiation medium

Dulbbecco's modified Eagle's medium (Gibco Co.) supplemented with 5% rabbit serum (Gibco Co.)

3. Plasmid for measurement of UCP-2 promoter activity

pGL3-basic (Promega Co.) plasmid DNA carrying UCP-2 promoter sequence of this invention and a structural gene (e.g. luciferase gene) inserted downstream of the UCP-2 promoter

4. Host cell line

MG-63 cells (osteosarcoma cell line, obtained from ATCC)

5. Test compounds

> Aqueous solutions are stored at 4°C or -20°C, and diluted to 1 μM with cell differentiation medium at use. Test compounds that are slight soluble in water are dissolved in dimethylforamide, DMSO, and methanol. [P. 16, ll. 4-33; all emphasis added.]

Applicants respectfully submit that, as noted in the specification, these are each an example of a given embodiment. An applicant is not necessarily limited to a specific set of conditions. One of ordinary skill in the pertinent art would understand, e.g., that another cell line might be used, which in turn might entail using a different culture medium.

The screening kit of the present invention may be a kit using a transformant that comprises a structure gene under control of a UCP-2 promoter of the present invention. Therefore, the kit may comprise a plasmid containing a UCP-2 promoter and a structural gene, a host cell, in which the plasmid is introduced and expressed, and a medium for culturing the cell. Amended claim 11 describes the plasmid in detail. Applicants respectfully submit that the descriptions of (1) the constitution of a UCP-2 promoter, (2) the structural gene, (3) animal cells used for a host and (4) media for culturing the cell are sufficiently definite. In addition, it is apparent that the medium can be used to culture the host cell or transformant. Thus, it is not necessary to include media for differentiation and for proliferation and maintenance. Further, it is unnecessary to include a compound for a test sample in the kit, especially as it would be expected that the user would provide such a sample precisely for the purpose of testing.

The kit of the present invention is practicable if the plasmid in the kit is introduced into the host animal cells to obtain a transformant and the transformant expresses a structural gene via the UCP-2 promoter. However, it is clear that the transformant that expresses a structural gene under control of the UCP-2 promoter can be obtained as described in the specification. Therefore, amended claim 11 meets the written description requirement.

Applicants respectfully submit that the present amendments to claim 11 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, first paragraph, thereby placing these claims in condition for allowance.

B. Rejection of Claims 1-8, 11, and 15-16 Regarding Written Description

The Examiner has rejected claims 1-8, 11, and 15-16 under 35 U.S.C. §112, first paragraph (pp. 7-9). Applicants respectfully disagree.

The Patent Office alleges:

> Claim 1 recites the term "uncoupling protein-2 (UCP-2) promoter region" and is directed to an isolated DNA comprising the UCP-2 region wherein the region comprises particular enhancer sequences (e.g. PPRE, C/EBP, GRE and MyoD-binding). Claim 11 recites the limitation of a reporter plasmid (i.e. pGL3-basic) comprising "the UCP-2 promoter sequence". While the instant specification discloses a nucleic acid sequence (SEQ ID NO: 1) that apparently comprises UCP-2 promoter activity, it does not disclose this sequence as setting the boundaries for what is considered the human UCP-2 promoter sequence. Moreover, there is no limitation in the rejected claims that the cited terms are limited to the human UCP-2 promoter, even if such boundaries were clearly defined in the instant specification for the human promoter sequence. While claim 4 recites that the isolated DNA comprises a UCP-2 promoter region comprising nucleotides 1-2270 of SEQ ID NO: 1, it also encompasses embodiments comprising only a fragment of nucleotides 1-2270 of SEQ ID NO: 1. A fragment of SEQ ID NO: 1 can be interpreted as being as small as a single nucleotide. Thus, the rejected claims read on an extremely large number of different nucleic acid sequences obtained from many different sources that are linked to regulation of expression of the uncoupling protein-2 gene.
>
> The instant specification is directed to the characterization of the ~2.3 kb hUCP-2 promoter fragment described by SEQ ID NO: 1 from nucleotides 1-2270. Very short sequences within this fragment were identified as well-known binding sites for different transcription regulators (e.g. the specifically recited oligonucleotide sequences recited in claim 1). Deletion constructs comprising portions of this region were made and the reporter gene activity determined....Thus, the instant specification does provide some data with regard to the basis organization and functional characteristics of the human UCP-2

promoter region described by nucleotides 1-2270 of SEQ ID NO: 1. On the other hand, there is no basis provided by the instant specification for one of skill in the art to envision what other sequences upstream from the described region might play a role in UCP-2 expression....

The UCP-2 sequence described by nucleotides 1-2270 of SEQ ID NO: 1 appears to have not been described in any great detail in the art at the time of filing.....Thus, the prior art fails to offset the deficiencies of the instant specification...

Given the enormous genus of UCP-2 promoter sequences encompassed by the rejected claims and the lack of any basis in the prior art or instant specification to envision other UCP-2 promoter sequences encompassed by the claims, the skilled artisan would not have been able to envision a sufficient number of specific embodiments of such UCP-2 sequences so as to describe the broadly claimed genus of such promoter sequences. Therefore, the skilled artisan would reasonably have concluded applicants were not in possession of the broadly claimed invention. [Pp. 7-9; emphasis in original.]

Claims 15 and 16 have been canceled without prejudice, and Applicants respectfully submit that the rejection is rendered moot with respect to these claims.

Applicants respectfully disagree, but have amended claims 1-6, 8, and 11. The language of claims 1 and 11 is as follows:

1 (currently amended). An isolated DNA comprising an uncoupling protein-2 (UCP-2) promoter region, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of:

a. a peroxisome proliferator response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;
b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;
c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and
d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1.

11 (currently amended). A kit for screening for a compound or its salt that promotes or inhibits UCP-2 promoter activity, which comprises:

a. a medium for culturing a host animal cell line;

b. a plasmid for measurement of UCP-2 promoter activity comprising:

i. plasmid DNA carrying a UCP-2 promoter sequence which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, which the part of the base sequence comprises a regulator sequence selected from the group consisting of:

(a) a peroxisome proliferators response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;

(b) a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1

(c) a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nuelcotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and

(d) a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1; and

ii. a structural gene inserted downstream of the UCP-2 promoter; and

c. a host animal cell line.

Applicants have amended claims 1 and 11 to refer to SEQ ID NO: 1. With respect to claim 4 and the other dependent claims, it should be noted that, because these claims are dependent on claim 1, they would also comprise a regulator sequence selected from the group listing in claim 1. Each of these groups has more than one nucleotide. While claim 4 has been amended to expressly claim sequences of more than one nucleotide, it is unclear how the Patent Office concludes that it would have covered a single nucleotide prior to amendment.

With respect to "other sequences upstream from the described region" and their role in UCP-2 expression, no support is cited for a requirement that the function of each and every base be described. Because the UCP-2 promoter region in amended claim 1 and the UCP-2 promoter sequence in amended claim 11 are specified (or limited) to all or part of the

base sequence from position 1 through 2270, the specification is not required to include teaching for other upstream sequences.

The Examples disclose each regulator sequence described in amended claim 1, and describe (1) preparation of seven deletion mutants, in which one or more regulator sequences were deleted, and (2) six mutants that maintained a promoter activity to varying degrees (except for the mutant in which all of the upstream region from the transcription initiation site is deleted). Because the UCP-2 promoter of the present invention may be utilized as a tool for screening a compound that regulates expression of UCP-2 by acting on any element in the regulatory region, Applicants respectfully assert that one of skill in the art can easily prepare, and use, any fragment containing a target regulator sequence.

Finally, as the Patent Office notes, in general, regulator sequences are highly conserved among species, such as animal species. Therefore, Applicants respectfully submit that it is possible to screen an agent for regulating an expression of UCP-2 in non-human, as well as human, animals using the human promoter sequence.

VI. The Rejection of Claims 1-8 Under 35 U.S.C. §102(b) Is Traversed

The Examiner has maintained the rejection of claims 1-8 under 35 U.S.C. §102(b) "as being anticipated by Surwit et al. (WO 98/31396; see the entire PCT application)." Applicants respectfully disagree.

The Patent Office reiterates the previous rejection and further alleges:

> The rejected claims are directed to a nucleic acid that comprises a UCP-2 promoter having the specifically recited binding elements of claim 1, recombinant vectors comprising the nucleic acid and host cells comprising the recombinant vectors. It is the examiner's contention, based on the reasons given

above, that the clones taught by Surwit et al would necessarily comprise at least one of the recited binding sites. The date that the sequence for the uncharacterized region that corresponds to applicants' claims is disclosed is irrelevant so long as Surwit et al were enabled for and had possession of the particular clones. There is nothing the examiner is aware of in the case law or in the statutes that says that the clones obtained by Surwit et al had to be deposited in order for the examiner to be able to use them as art, or conversely, that the deposited material cannot be used as art. As the response correctly points out, the deposited material satisfies the requirements of 112 1st paragraph with regard to enablement and description. With regard to the observation that there is a "certain degree" of variance between the disclosed sequences taught by Surwit et al and the sequences disclosed in the instant specification, the location and degree of variance is never described in applicants' response, making it difficult to extrapolate that variance to the regions specifically recited in the rejected claims. Moreover, there is reason to expect that while there might be variance in the broad region of the nucleic acid sequence not explicitly disclosed by Surwit et al from applicants' own data, this variance is actually unlikely to extend into the specifically recited enhancer sequences described by applicants. These sites are very short sequences that are extraordinarily well conserved across multiple different types of genes obtained from many different animal species (e.g. as evidence of this conservation of sequence, see the attached sequence search results for sequences described within issued patents; Exhibits A-H). Further, applicants' own data suggests that at least three of the sites actually do play a role in regulation of UCP-2 expression (e.g. Example 4), indicating that those particular enhancer sites are important to UCP-2 gene regulation and are, therefore, even more likely to be conserved. It is exceedingly unlikely, given the facts outlined above and this conservation in sequence across species for many very different genes, that the specifically recited enhancer sites are not present in the clones disclosed by Surwit et al. Thus, one of skill in the art would necessarily expect that the deposited material would meet the structural/functional limitations for the UCP-2 promoter regions of the rejected claims.

The teachings of Surwit et al (WO 98/31396 Al) are also disclosed in U.S. 2003/0119775 Al. The U.S. application does not appear to comprise a sequence listing that discloses the relevant sequences so that the examiner could do the comparison for applicant. The examiner would be glad to do so if it were possible. However, arguments directed to an undue burden placed on applicants in independently determining the sequence of the clones disclosed by Surwit et al are irrelevant. Applicants' response has not effectively rebutted the examiner's argument that one would necessarily expect the clones disclosed by Surwit et al to possess the recited structural and functional characteristics. As indicated above, the Office does not have the facilities for examining and comparing the applicants' product with the products of the prior art, and the burden is on the applicants to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional

characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicants respectfully disagree with these comments, in addition to those from the previous Office Action, and traverse the anticipation rejection.

As noted, the present language of claim 1 reads as follows:

> 1 (currently amended). An isolated DNA comprising an uncoupling protein-2 (UCP-2) promoter region, which comprises all or part of the base sequence consisting of nucleotides 1 to 2270 of SEQ ID NO: 1, wherein the part of the base sequence comprises a regulator sequence selected from the group consisting of:
>
> a. a peroxisome proliferator response element (PPRE) sequence comprising nucleotides 284 to 296 of SEQ ID NO: 1;
> b. a CCAAT/enhancer binding protein (C/EBP) sequence comprising nucleotides 1316 to 1320 of SEQ ID NO: 1, nucleotides 1364 to 1368 of SEQ ID NO: 1, or nucleotides 1698 to 1692 of SEQ ID NO: 1;
> c. a glucocorticoid response element (GRE) sequence comprising nucleotides 753 to 758 of SEQ ID NO: 1, nucleotides 1023 to 1030 of SEQ ID NO: 1, or nucleotides 1450 to 1455 of SEQ ID NO: 1; and
> d. a MyoD-binding sequence comprising nucleotides 1428 to 1437 of SEQ ID NO: 1.

Applicants respectfully submit that claim 1 in its present form is not anticipated by Surwit (WO 98/31396). The present application discloses promoter activity for the human UCP-2 gene and provides specific regulator sequences and experimental data regarding the same, including deletion mutants (see, e.g., p. 14, l. 1, to p. 15, l. 2, and the Examples).

In Surwit, a promoter sequence is partially disclosed. A 14 kb human DNA is described, which "contains all the 8 exons and introns, and a minimum of 3 kb of DNA upstream of the putative +1 site" (p. 32, ll. 25-27). Four regions of this clone were sequenced. Specifically, the Sequence 2 of Figure 10B, which is a sequence containing a transcription initiation site, appears to correspond to a portion of the present invention, but

the two sequences are not identical and display a certain degree of variation. The first nucleotide of Sequence 2 appears to correspond to about the 1730th nucleotide of SEQ ID NO: 1 of the present application. The specification of Surwit states that "Sequence 2 corresponds to a 1161 bp DNA from positions BP –511 to +650" and that "this fragment contains the putative proximal human UCP2 promoter" (p. 33, ll. 3-5). In addition, the Sequence 1 of Figure 1A appears to be upstream of the sequence of the present invention. Surwit states that "Sequence 1 corresponds to 640 bp of DNA forming the 5' extremity of the human [UCP2] DNA" (p. 33, ll. 1-3). The "5' extremity" is "a miniumum of 3 kb of DNA upstream of the putative +1 site," which is upstream of the sequence of SEQ ID NO: 1 of the present invention. (According to Figure 9 of Surwit, Sequence 3 (Figure 10C) and Sequence 4 (Figure 10D) are downstream of the +1 site.) Further, Surwit does not clearly disclose the sequence between Sequence 1 and Sequence 2, which is where the regulator sequences specified in claim 1 would be located.

With respect to claim 1, the publication of Surwit does not include a sequence listing. As a result, the sequences recited in claim 1 are not clearly included in the disclosure of Surwit.

Applicants respectfully submit that it is impossible to consider the undisclosed sequence between Sequence 1 and Sequence 2 of Surwit. For reasons discussed at length in the Amendment filed on December 22, 2004, the Patent Office has not established prima facie anticipation or obviousness of these sequences and their respective classifications by Surwit.

Applicants' arguments already of record are not reiterate here, but Applicants respectfully submit that these arguments continue to apply.

Applicants respectfully assert that requiring Applicants to obtain one or more cell lines of Surwit and then to isolate, clone, and sequence the DNA in order to compare it with Applicants' DNA is unduly burdensome. In *Enzo*, the question was whether a deposit in a public depository constituted an adequate description to comply with 35 U.S.C. §112, ¶1 (Enzo Biochem. v. Gen-Probe, 296 F.3d 1316 (Fed. Cir. 2002) – not whether a biological deposit could be used as prior art against a third party for purposes of anticipation (35 U.S.C. §102) or obviousness (35 U.S.C. §103). Such a holding would be unduly burdensome to practitioners. Applicants respectfully submit that the Patent Office has not yet taken into consideration this distinction vis-à-vis *Enzo*.

Applicants respectfully reiterate that if, as designated on the cover sheet of the PCT application, Surwit has since been filed in the U.S. Patent & Trademark Office, either as a national phase application under 35 U.S.C. §371 or as a *bona fide* continuation or divisional, then the Patent Office should have required submission of an electronic copy of the sequence listing of Surwit, in addition to the electronic copy submitted for the present invention, and would be in the best position to compare the two sequences.

Moreover, Applicants have compared the sequence of the present application with the sequences disclosed in Fig. 10B and Fig. 10C of Surwit and have attached this sequence alignment comparison herewith (Exhibit A). As a result, it can been seen that the sequence at position of 2328-2357 of SEQ ID NO: 1, consisting of 30 bases, is deleted from the sequence of Surwit. If other deletions exist within the regulator sequence region not included in the cited reference, then deletion of one or more regulator sequence could occur. Accordingly, whether or not the regulator sequence of the present application is included in the clone of Surwit is not clear without sequencing the corresponding region of the clone. Moreover, it is possible that the deletion is due to a cloning artifact, rather than to a deletion from the genome. As a result, Applicants respectfully submit that there is a high probability of deletion of the regulator sequence in the Surwit clone.

Therefore, Applicants respectfully submit that the Patent Office has not met the burden of proof for making a prima facie showing that the sequences recited in claim 1 are expressly disclosed in Surwit.

Claims 2-8 are dependent on claim 1, and the same arguments apply to these claims as well.

Applicants respectfully submit that the present claims 1-8 fulfill the requirements of 35 U.S.C. §102(b) and request the Examiner's reconsideration of these claims accordingly.

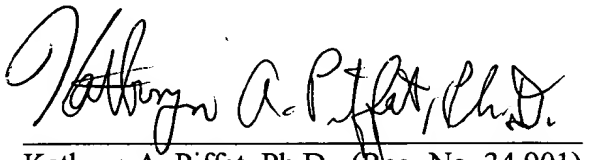
VII. Conclusion

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a three-month extension of time for the Amendment and accompanying materials. If an additional extension of time is required, Applicants hereby request the Examiner to consider this a conditional petition for an extension of time. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,



Date: October 7, 2005

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Customer No. 21874
BOS2_511449.1

83.3% identity in 1191 residues overlap; Score: 5584.0; Gap frequency: 5.7%

```
SEQ ID NO:1   1733 AGGAGCCAGCCGCGCGCTCGCTCGCAGGAGGGTGGGTAGTTTGCCCAGCG--TAGGGGGG
Fig. 10B         2 ANGAACCACCGGCGCGTTCGTTCGCAGGAGGTTGGTTAGTTTGCCCAGGGGTAAGGGGGG
                   * ** *** * ***** *** ********** *** ********** *   *******

SEQ ID NO:1   1791 CTGGGCCCATAAAAGAGGAAGTGCA-CTTAAGACACGGCCCC-GCTGGACGCTTGTTAGA
Fig. 10B        62 CTGGGCCCATAAAAGAGGAAGTGCAACTTAAGACACGGCCCCCGTTGGACGCT-GTTAGA
                   ************************ *************** * ******** ******

SEQ ID NO:1   1849 AACCGTCCTGG-CTGGGAAGGCAAGAGGTGTGTGACTGGACAAGACTTGTTTCTGG-CGG
Fig. 10B        121 AACCTTCCTGGGTTGGGAAGGCAAGAGGTGTGTGACTGGACAAGAATTGTTTCTGGGCGG
                   **** ******  ********************************** ********** ***

SEQ ID NO:1   1907 TCAGTCTTGCCATCCTCACAGAGGTTGGCGGCCCGAGAGAGTGTGAGGCAGAGGCGGGGA
Fig. 10B        181 TCAGTCTTGCCATCCTCACAGAGGTTGGCGGCCCGAGAGAGTGTGAGGCAGAGGCGGGGA
                   ************************************************************

SEQ ID NO:1   1967 GTGGCAAGGGAGTGACCATCTCGGGGAACGAAGGAGTAAACGCGGTGATGGGACGCACGG
Fig. 10B        241 GTGGCAAGGGAGTGACCATCTCGGGGAACGAAGGAGTAAACGCGGTGATGGGACGCACGG
                   ************************************************************

SEQ ID NO:1   2027 AAA-CGGGAGTGGAGAAAGTCATGGAGAGAACCCTAGGCGGGGCGGTCCCCGCGGAAAGG
Fig. 10B        301 AAAACGGGAGTGGAGAAAGTCATGGAGAGAACCTTAGGCGGGGCGGTCCCCGCGGAAAGG
                   *** ************************** ************************

SEQ ID NO:1   2086 CGGCTGCTCCAGGGTCTCCGCACCCAAGTAGGAGCTGGCAGGCCCGGCCCCGCCCCGCAG
Fig. 10B        361 CGGCTGCTCCAGGGTCTCCGCACCCAAGTAGGAGCTGGCAGGCCCGGCCCCGCCCCGCAG
                   ************************************************************

SEQ ID NO:1   2146 GCCCCACCCCGGGCCCCGCCCCCGAGGCTTAAGCCGCGCCGCCGCCTGCGCGGAGCCCCA
Fig. 10B        421 GCCCCACCCCGGGCCCCGCCCCCGAGGCTTAAGCCGCGCCGCCGCCTGCGCGGAGCCCCA
                   ************************************************************

SEQ ID NO:1   2206 CTGCGAAGCCCAGCTGCGCGCGCCTTGGGATTGACTGTCCACGCTCGCCCGGCTCGTCCG
Fig. 10B        481 CTGCGAAGCCCAGCTGCGCGCGCCTTGGGATTGACTGTCCACGCTCGCCCGGCTCGTCCG
                   ************************************************************

SEQ ID NO:1   2266 ACGCGCCCTCCGCCAGCCGACAGACACAGCCGCACGCACTGCCGTGTTCTCCCTGCGGCT
Fig. 10B        541 ACGCGCCGTCCGCCAGCCGACNGACACGGCCAAACGAAAGGNNCCNNNNNCCCTGCGGCT
                   ******* ************ ***** ***  *** *  *         **********

SEQ ID NO:1   2326 CGGTGAGGCTGGCCCCAGCCCTGCGCCCTTTGCGCCCCCCACGCTTGTTCTGCGTGCGCT
Fig. 10B        601 CG                                CGNACCCCACGCTTGTTCTGCGTGCGCT
                   **                                ** ************************
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SEQ ID NO:1   2386 GCCCGCTCTTCCATTTACCTTCTCTCCCACCCAAGTTTGTACTCTTTTCTTTCTCTCGGT
Fig. 10B       631 GCCCGCTCTTCCATTTACCTTCTCTCCCACCCAAGTTTGTACTCTCTTCTCTCTCTCGGT
                   ********************************************** **** *********

SEQ ID NO:1   2446 TTTATTTTTTGTTTTTGTTTGTTTGTTTGAGACAGGCTTTCGCTCTGTCTCCCAGGCTGG
Fig. 10B       691 GTTATATTTTGTGTTTGTGTGTGTGTGTGAGACAGGCGCTCGCTCTGTCTCCCACGCTGG
                    **** ****** ***** *** *** **********  ********************

SEQ ID NO:1   2506 AGTG-CAGTGGCGCGATCTCGGCTCACTGCAGCCTCCACCTCCCAGGTTCAAGCGATCCG
Fig. 10B       751 AGTGTCAGTGGCGCGATATCGGCTCACTGCAGACTCCACCTCCCAGGTGNAAACGATNCG
                   **** ************ ********************** ***************  ** **** **

SEQ ID NO:1   2565 CCTGCCGAGTAGCTGGGATTACAGGCGCCCGCCACCACGCC-TGGCTAATTTTTGTGT--
Fig. 10B       811 CCTGCCGAGTATCTGGGATAACAGGCGCCCGCCACCACACCCTGGCTAATATTTNTGTGT
                   *********** ******* ****************** ** ******** *** ***

SEQ ID NO:1   2622 -TTTGTAGAG-ATGGGGT-TTCGCC-ATGTTGGC-CAGGCTGG--CCTCGAACTGCTCAG
Fig. 10B       871 GTTTGTANAANATAGGGTGTTCGCCCACGTTGGTGCAGGCTGGNCTCTCAANTTGCTGAG
                    ****** *  ** **** ****** * *****  ********   *** *  **** **

SEQ ID NO:1   2675 CT-CAAGCAATCCGCCCGCC-TCGGC-CTCACAAA--GTC-CTAGAAT-TTTAGGCATGA
Fig. 10B       931 ATTCAAGCAATNTGCCCGCCCTCGGNGCTCACAAAAAGTCNCTANAAANTTTAGGCGTGA
                    * ********  ******* ****  ********  *** *** **  ******* ***

SEQ ID NO:1   2728 G--CCTCCGGGTCCGGCCTGT-GCTAAT---CCTTTCTGTCCTTGGTTCTTTATTTCC--
Fig. 10B       991 AACCCCCCGGTNNNGGGCTGTTGCTAAANCNCCTCNTGTCCCTGGGGNCTCTAAAANCTN
                      ** ****    ** **** *****    ***      *** **  ** **    *

SEQ ID NO:1   2780 CTTCTCTCTT-TTTCTTAGTCCCTTTTGTTCTTT-CCCTCTCCCGTTCAGTTGGCTG-TC
Fig. 10B      1051 CTNCACTCCTCTTTCCTCAATCCCCTTGTTCTTTTCCCCCNCCCGCTCAATTNGNNGGTN
                   ** * *** * **** *    **  ********* *** * **** *** ** *  * *

SEQ ID NO:1   2837 GTTTGAGCCTCCACCTTTTCACT-CCCTCCTTTCCACCACGATGCCGAGCC
Fig. 10B      1111 NTTTGANNCNCCNCCTTTTNAATNCCCNCCTTTNCANAANNAAAACTAACC
                    *****  * ** ****** * * *** ***** **  *  *   * * **
```

90.3% identity in 505 residues overlap; Score: 2541.0; Gap frequency: 3.4%

```
SEQ ID NO:1   3018 TGGCCTCTGC-AGGGCC-GGCTCCCAG-CCCTTCCAACCT--CCTCACAGCCCGACCT--
Fig. 10C         3 TGGCCTTGGGNAGGGCCNGGTTCCCAGNCCTTTCCAAACTTTCTTNACAGCCCGGACGNG
                   ******  *  ****** ** ****** ** ****** **  * * ********  *

SEQ ID NO:1   3071 GGGACCTA-GCCAATTCCCGGAGAGTCTCT---GTCCCA-TCGTGACCCCCT--CACAAC
Fig. 10C        63 GGGACNTAAGCCAATTTCCGGGGAGAGTTTNTGGTCCCANTGGNGACCCCCTTNAAAAAT
                   ***** ** ******* **** ***  * *   ****** * * ********   * **

SEQ ID NO:1   3124 TCTCCCACTCACCAAAGTCTGATG-ACTGTGCTAGGGGGTGCTTATATAGAGTACTGAGT
Fig. 10C       123 TTTCCNATTNACCAAAGTNTGATGGACTGNGTTAGGGGGTGCTTATATAGAGTACTGAGT
                   * *** * * ******** ***** **** * **************************

SEQ ID NO:1   3183 GTTACAAAAGCAGAAGTCTGGATGAGAACC-AATTTGTGATATTAAGCAGGTGGGGTGGG
Fig. 10C       183 GTAACAAAAGCAGAAGTCTGGATGAGAACCCAATTTGTGATATTAAGCAGGTGGGGTGGG
                   ** ************************* ****************************

SEQ ID NO:1   3242 GGTGGGGAGTGTACCTAGGTTCATTTTCCGCCCTGCTTTTCCCCTTTCCAGTGTGTGCAC
Fig. 10C       243 GGTGGGGAGTGTACCTAGGTTCATTTTCCGCCNTGCTTNTCCCCTTTCCAGTGTGTGCAC
                   ******************************** ***** ********************

SEQ ID NO:1   3302 TTAACCAGT-CCCTGGGCCCTGTTCCCCATCCCCCTCCAAGGCATGGATTGGGTGGGCTT
Fig. 10C       303 TTAACCAGTTCCCTGGGCCCTGTTCCCCATCCCCCTCCAAGGCATGGATTGGGTGGGCTT
                   ********* ************************************************

SEQ ID NO:1   3361 GTGTGTCTTGGGGCAGGTGGCCCTTTCTAAACTCTCTGCCTTTGCTCACCCACAGGACAC
Fig. 10C       363 GTGTGTCTTGGGGCAGGTGGCCCTTTCTAAACTCTCTGCCTTTGCTCACCCACAGGACAC
                   ************************************************************

SEQ ID NO:1   3421 ATAGTATGACCATTAGGTGTTTCGTCTCCCACCCATTTTCTATGGAAAACCAAGGGGATC
Fig. 10C       423 ATAGTATGACCATTAGGTGTTTCGTCTCCCACCCATTTTCTATGGAAAACCAAGGGGATC
                   ************************************************************

SEQ ID NO:1   3481 GGGCCATGATAGCCACTGGCAGCTT
Fig. 10C       483 GGGCCATGATAGCCACTGGCAGCTT
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